

REMARKS/ARGUMENTS

Claims 1-26 are currently pending in the above-identified application. Claims 11-13, 15, 19, 21, and 24-26 have been amended. Claims 1-10, 14, 16, 20, and 23 have been canceled without prejudice to Applicant's right to prosecute the subject matter of the claims in this or a related, co-pending application. Support for these amendments is identified in the following remarks. No new matter is added by these amendments.

Rejections under 35 U.S.C. §112

Claims 1-13, 15, 20-21, and 23 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner believes that the use of the term "agent" as recited in claims 1-13 and 15 is ambiguous. Although Applicants do not agree with the Examiner's reasoning, but to further expedite prosecution of certain subject matter disclosed and claimed in the application, Applicants have canceled claims 1-10, 20 and 23 without prejudice. Further claims 11 and 15 have been amended to replace the term "agent" with the term "composition" as suggested by the Examiner. Claims 12 and 13 are dependent on claim 11 and therefore also contain the same amendment.

Further the Examiner believes the use of the term "derivative" in Claims 8, 20, 21 and 23 is ambiguous since "derivative" as used is believed to refer to material derived from the named formula while it is believed that the material disclosed by Applicant are believed to be the named formula. Although Applicants do not agree with the Examiner's interpretation of the present invention, but in order to further expedite prosecution of certain subject matter disclosed and claims in the application, Applicants have canceled claim 8, 20 and 23 without prejudice. Further, claim 21 has been amended to replace the term "derivative" with the term "composition" as suggested by the Examiner.

Also, the Examiner does not appear to understand the language "binds to the hydrophobic pocket of the Bcl-2 family member ... formed by BH1, BH2 ... domains of the protein." Applicants believe that the language is well understood in the art. As described beginning at page 1, line 29, the Bcl-2 family member proteins comprise several conserved amino acid motifs. The motifs are identified as BH1, BH2, BH3 and BH4. A description of the hydrophobic pocket is found for example at page 2, lines 4 through 7 of the specification as filed. Further, claim 15 has been amended to recite only the Bcl-x_L or Bcl-2 members of the Bcl-2 family and therefore Applicants believe that the claims are definite and distinctly claim the subject matter which Applicants' regard as the invention.

The Examiner has also noted that for claim 11 the first chemical modification provides no definition for R₁, R₂, R₃, or R₆, while under the second chemical modification there is no definition for R₄ or R₅. While Applicants believe claim 11 to be understandable as filed, but in order to further expedite prosecution of certain subject matter disclosed and claimed in the application, claim 11 has been amended to delete the reference to a first and second chemical modification and to recite a composition of formula II having an absolute configuration of [2R, 3R, 4S, 7S, 8R wherein R₁ through R₆ are as recited in the claim. The definitions for R₄ and R₅ have been moved to follow the definition for R₃.

Still further, the Examiner has noted that claims 4 and 23 recite as a species the compound of formula VII. The Examiner does not believe that proper antecedent basis for this species can be found in claims 3 or 21 respectively. Applicants believe that this rejection has been mooted by the cancellation of claims 4 and 23 without prejudice.

Claims 1, 5, 6, 9-11, 13-15, 17, and 20 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The Examiner believes that the claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and/or use the invention. In particular, the Examiner believes that the prior art of the

claimed invention is that comprising screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities. The Examiner further believes that this art does not provide absolute predictability even in view of the seemingly high level of skill in the art. As such, the Examiner has questioned "[w]hat is the scope of the term "modulates apoptosis"? and what is the scope of "apoptosis-associate disease"? Therefore, the Examiner does not believe the specification reasonably provides enablement for the scope of the present claims which encompass using compounds of formula II to treat all possible apoptosis-associated diseases.

Further, the Examiner does not believe that a correlation between the tests disclosed in the specification and the claimed utility of "modulating apoptosis" or "identifying agents which modulate apoptosis", or "treating a subject with an apoptosis-associated disease". Therefore, the Examiner does not believe the specification provides sufficient support for the use of the compounds of claim 1 for modulating apoptosis, treating a subject with an apoptosis-associated disease, or identifying an agent which modulates apoptosis. It should be noted that the Examiner has objected to Claims 14, 16-19, 22, and 24-26 as being dependent upon a rejected base claim, but that the claims would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicants do not agree with the Examiner's remarks or conclusions related to enablement, but in order to further expedite the prosecution of certain subject matter disclosed and claimed in the present application, Applicants have cancelled claims 1-10, 14, 16, 20 and 23. Claims 11-13, 15, 19, 21 and 24-26 have been amended to encompass the subject matter of claims 14, 16-19, 21 and 24-26. In particular, claim 11 has been amended to recite an apoptotic composition that induces apoptosis by binding to a Bcl-2 family member protein in a cell that over-express the Bcl-2 family member protein, the composition having the following formula II. This amendment incorporates the limitations of claim 14 into claim 11. The Examiner has indicated that the subject matter of claim 14 was allowable.

Further, Claim 15 has been amended to recite a method for identifying a composition which induces apoptosis of a cell by binding to the hydrophobic pocket of Bcl-x_L or Bcl-2 formed by the BH1, BH2, and BH3 domains of the protein. The method comprises admixing a candidate compound with a cell which over-expresses Bcl-x_L or Bcl-2; admixing the candidate compound with a control cell which does not over-express the Bcl-x_L or Bcl-2; and determining whether the candidate compound induces the activity of the Bcl-x_L or Bcl-2 protein to produce a physiological change in the cell which over-express the Bcl-x_L or Bcl-2 protein indicative of apoptosis, but does not produce a substantial physiological change in the cell which does not over-express the Bcl-x_L or Bcl-2. The amendments to claim 15 incorporate the elements of claim 16 which the Examiner has indicated is allowable. Claim 16 has been cancelled and claims 17-19 are dependent on claim 15.

Also, claim 20 has been cancelled without prejudice and claim 21 has been amended to be independent incorporating the preamble of claim 20 and to recite wherein the antimycin or antimycin composition is of the recited configuration and formula. Applicants believe that the method of the invention is fully enabled for the recited method using the scope of compounds of amended claim 21. In particular, apoptosis-associated disease as used in the present context are those disease requiring the induction of apoptosis of cell which over-express a Bcl-2 family member protein. Further, claims 22 and 23 have been cancelled without prejudice and claims 24-26 have been amended to change the dependency of the claims to claim 21.

Applicants believe that each issue raised by the Examiner has been addressed. It is respectfully requested that the Examiner reconsider and withdraw the rejections of claims 1-13, 15, 20, 21 and 23 under 35 U.S.C. § 112, first and second paragraph, in light of the amendments and remarks.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an

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Appl. No. 10/069,431
Amdt. dated September 6, 2005
Reply to Office Action of May 5, 2005

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early date is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

Dated: 6 September 2005

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